

### **REMARKS**

Claims 1-11 are currently pending. Claim 4 is currently amended to correct a typographical error.

#### **Claim Rejections - 35 U.S.C. § 103(a)**

In the Final Office Action mailed October 2, 2008, the Examiner maintained their rejection of claims 1-11 under 35 U.S.C. § 103(a) as being unpatentable over Thomas (U.S. Patent No. 5,811,446) in view of Blackburn *et al.* (U.S. Patent No. 4,980,163, hereinafter “Blackburn”). Applicants respectfully traverse the rejection.

The Examiner alleges that the problem to be solved is the treatment of blepharitis and that there are a limited number of methodologies for doing so. Therefore, the Examiner, citing *KSR v. Teleflex Inc.* 127 S. Ct. 1727 (2007), contends that the “obvious to try” test is a proper test for determining the patentability of the presently claimed invention. The Examiner alleges that because there are a limited number of methodologies for treating blepharitis, it would have been obvious to one of ordinary skill in the art to try the bacteriocin composition of Blackburn in Thomas’ method of treating blepharitis with the reasonable expectation of deriving the presently claimed invention.

In order to reject a claim under the “obvious to try” rationale the Examiner must establish at least the following: 1) a finding at the time of the invention there had been a recognized problem or need in the art; 2) a finding there had been a finite number of identified, predictable potential solutions; and 3) a finding that one of ordinary skill in the art could have pursued the known potential solutions with a reasonable expectation of success (Federal Register, Vol. 72(195), page 57532).

Applicants respectfully submit the Examiner has misunderstood the nature of the problem to be solved. The present claims are directed to a method of treating dry eye disease. Dry eye disease results from abnormalities of the precorneal tear film characterized by a decrease in tear production or an increase in tear film evaporation (See page 1, lines 17-19 of the specification). Therefore, one of ordinary skill in the art would recognize that the problem to be solved is not

the provision of an antibiotic for treating a bacterial infection, but instead the provision of a compound that can increase or restore deficits in tear film production.

As a result of mischaracterizing the problem to be solved, Applicants respectfully submit the Examiner has also not established that there were a finite number of identifiable and predictable solutions for treating dry eye disease. Thomas does not suggest that any antibiotic, much less lantibiotics, are capable of increasing tear film production. All of the exemplified antibiotics listed in column 8, lines 7-14, are referenced solely for their antibiotic activities, not their ability to increase tear film production. Similarly, Blackburn only teaches the antibiotic properties of nisin and lysostaphin and how these properties can be enhanced when used in combination. Applicants submit that it cannot be argued that there are a finite number of identifiable and predictable solutions when neither Blackburn or Thomas has established that lantibiotics can be used for increasing tear film production.

Further, Applicants submit that, regardless of the rationale used, the Examiner has not established a reasonable expectation of success. The Examiner concedes that Thomas teaches away from the use of beta-lactams and fluorquinolone. However, the Examiner contends this would only motivate one of skill in the art to look at other classes of antibiotics. The Examiner alleges that Thomas suggests that broad range antibiotics in particular would be useful in treating ocular infections. Thomas teaches that histidine may be useful in treating inflammation associated with ocular diseases and trauma (Column 4, lines 27-37). Since inflammation is a common sequela of many ocular diseases (Column 4, lines 55-57), Thomas suggest that it may be useful to co-administer histidine with "a broad range of presently available ocular therapeutics" (Column 7, lines 52-55). Nowhere does Thomas specifically suggest that broad range antibiotics would be a desirable option in treating ocular infections. Therefore, the Examiner's assertion that one of ordinary skill in the art would be motivated to try broad range antibiotics based on the teaching of Thomas is factually incorrect. In addition, the issues raised by Thomas regarding toxicity and effectiveness of antibiotics in treating ocular infections cannot be ignored. The prior art must be considered in its entirety, including disclosures that teach away from the claims. Given the toxicity and effectiveness issues raised by Thomas, it cannot be argued that one of ordinary skill in the art would have a reasonable expectation of successfully

substituting any one class of antibiotics for another without some evidence of that antibiotic's effectiveness and safety in treating ocular infections. On this point the cited art is clearly lacking. Thomas merely suggest the use of histidine in combination with any number of proven ocular therapeutics (Column 7, lines 52-55), and Blackburn is silent on the effectiveness of nisin and lysostaphin, either alone or in combination, for treating ocular diseases. Therefore, one of ordinary skill in the art would not have a reasonable expectation of success in deriving the presently claimed invention based on the teaching of Blackburn and Thomas.

As further evidence of nonobviousness, the present application demonstrates unexpected results. In contrast to the cited art, the present application demonstrates that administration of the claimed lantibiotics unexpectedly increases tear flow. Examples 1 and 2 and Table I of the present application demonstrate that administration of a lantibiotic is capable of increasing tear production using a Shirmer test. The Schirmer test is an art recognized assay for evaluating tear secretion in response to conjunctival stimulation and basal, non-reflex secretion (Schirmer O. Graefes Arch Clin Exp Ophthalmol. 1963, 56:197-291). The fact that lantibiotics could increase tear secretion was completely unexpected based on the disclosures of Thomas and Blackburn, as this activity is unrelated to any antibiotic effect.

Applicants respectfully submit, that given the above, the application of a "obvious to try" test was improper. The Examiner did not correctly identify the problem to be solved nor establish that there were a finite number of identifiable and predictable solutions, or that one of ordinary skill would have a reasonable expectation of success in combining the cited references. Further, Applicants submit that based on the prior art, as evidenced by Thomas and Blackburn, the ability of lantibiotics to increase tear film production was unexpected and as such renders the presently claimed invention non-obvious over the cited prior art. For at least the foregoing, Applicants submit the rejection under 35 U.S.C. § 103(a) has been overcome and respectfully request that it be withdrawn.

### **Claim Rejections - Double Patenting**

The Examiner provisionally rejected claims 1-11 on the grounds of non-statutory obviousness-type double patenting as unpatentable over claims 1-8 of copending U.S.

Application No. 11/123,436 (hereinafter “the ‘436 application”). The ‘436 application issued as U.S. Patent No. 7,479,481 on January 20, 2009. Applicants file herewith a terminal disclaimer disclaiming the terminal portion of any patent to issue from the present application that would extend beyond the term of U.S. Patent No. 7,479,481. Applicants submit the filing of the terminal disclaimer obviates the rejection on the grounds of non-statutory obviousness type double patenting.

### **CONCLUSION**

The foregoing is submitted as a full and complete response to the Final Office Action mailed October 2, 2008, and early and favorable consideration of the claims is requested. If the Examiner believes any informalities remain in the application that may be corrected by Examiner’s amendment, or there are any other issues which can be resolved by telephone interview, a telephone call to the undersigned agent at (404) 572-2447 is respectfully solicited. No additional fees are believed due; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 11-0980.

Respectfully submitted,

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